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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/569,797	11/20/2006	Uwe Fiebig	GULDE-0068	6634

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EXAMINER	
SNYDER, STUART	
ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/569,797	FIEBIG ET AL.	
	Examiner	Art Unit	
	STUART W. SNYDER	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 August 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,13-18,21,22,25 and 29-42* is/are pending in the application.

4a) Of the above claim(s) *18,21,22,25,29-32,36 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,13-17,33-35 and 37-42* is/are rejected.

7)☒ Claim(s) *9* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/27/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I (claims 1-10, 13-17 and 33-41) in the reply filed on 1/28/2008 is acknowledged; applicants further elected gp41 and HIV-1 as species for initial examination.

The traversal is on the ground(s) that Groups relate to one general inventive concept. This is not found persuasive because the common concept of the claimed inventions is not inventive having been anticipated by Okuda, *et al.* As such, the claimed invention lacks unity under PCT Rule 13.2.

The requirement is still deemed proper and is therefore made FINAL.

Claims 18, 21-22, 25, 29-32, 36 and 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions and/or species, there being no allowable generic or linking claim.

Claim Objections

2. Claim 9 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 9 recites "[a] pharmaceutical agent" in reference on an immunogenic construct of claim 1. However, additional structural limitations are imposed on the construct of claim 1 and thus, claim 9 does not further limit claim 1.

Specification

3. The disclosure is objected to because of the following informalities: On page 57, the heading "Legends" appears. However, Applicants are required to include a section entitiled "Brief Description of Figures".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 39 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claim is drawn to a peptidyl agent for prophylactic or therapeutic treatment of an HIV infection. For unknown reasons, no peptide-based prophylactic of therapeutic treatment has been developed to date nor has Applicants provided data demonstrating that such a construct has been developed (see, Levine, 2008, for detailed analysis on failure of anti-HIV vaccine, to date). Enablement is considered in view of the Wands factors (MPEP 2164.01 (a)).

Nature of the invention. The instant invention is drawn to a vaccine for HIV. The term "vaccine," by definition, implies a preparation intended for active

immunological prophylaxis. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease.

State of the prior art. It is well known in the art and even to the general public that medical science, despite decades of intense research, has not found any antigen, immunogen, or compound that can be credibly used as a vaccine against HIV.

The difficulties inherent to developing an HIV vaccine are well known. For the sake, of clarity, some of those problems are outlined here:

1) the extensive genomic diversity associated with HIV, due in large part to error prone reverse transcription of its RNA genome,
2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form (cell to cell transmission), as well as via free virus transmission,
3) the existence of latent forms of the virus,
4) the complexity and variation of the elaboration of the disease, and
5) the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences.

The existence of these obstacles prevents one of ordinary skill in the art from accepting any therapeutic regimen on its face given the intense interest in developing HIV treatments or vaccines and the lack of success in doing so.

Working examples. The specification contains examples showing the immunogenicity of various preparations and examples where sera so produced

"neutralized" virus *in vitro*. None of the examples, however, show protection in vivo; e.g., there are no examples showing vaccination Applicants' immunogen and challenge with HIV resulting in protection, prevention or amelioration of HIV infection.

Guidance in the specification. The claimed invention is directed to immunogenic preparations derived from HIV-1 gp41 and homologues. There is insufficient disclosure to reasonably predict that the claimed vaccine of the instant specification would prevent or ameliorate an HIV infection. In addition, the disclosure fails to provide any guidance pertaining to the correlates of human protection. To date, it is not clear what type of immune response is required to provide a therapeutic benefit.

Predictability or unpredictability of the art. The state-of-the-art vis-à-vis HIV vaccine development is one of unpredictability (see, Levine, 2008). To date, there is not one single effective HIV vaccine on the market. Several clinical trials have been conducted but in every situation, the immunogen failed to induce a long-lasting and high-titer immune response.

Accordingly, when all the aforementioned factors are considered *in toto*, it would require undue experimentation for one skilled in the art to practice the claimed invention.

Working Examples: The disclosure fails to provide any working embodiments; i.e., an immunogen that protects from or ameliorates a viral infection.

For the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods. Therefore, the claimed invention lacks an enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-10, 13-17, 33-35 and 37-41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites:

> "An immunogenic construct comprising amino acid sequences selected from a viral transmembrane envelope protein of one virus which is associated with the viral membrane via at least one transmembrane region and comprises at least one fusion domain and at least two [alpha]-helical structures, characterized in that wherein the amino acid sequences are selected from:"

It is unclear from the language and punctuation used in the claim whether it is the viral protein or the immunogenic construct that must possess "one fusion domain and at least two [alpha]-helical structures". Either interpretation of the claim is supported by the specification, however the later places at least three constraints (one fusion and two alpha-helical domains) on the structure of the claimed construct whereas the former interpretation only places two constraints on the claimed construct (two alpha-helical domains). Thus, the structure of the claimed construct in unclear.

6. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 provides for the use of the immunogen of Claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

7. Claim 10 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

8. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 recites "at least one sequence of Nos. 1 to 104". Although the specification provides sequences for SEQ ID NO.s 1-104, such language is not found in the specification, and unless there was an unintentional omission of the phrase "SEQ ID" in the claim, the aforementioned reference to Nos. 1 to 104 is ambiguous and does not have literal support in the specification.

9. Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 10 provides for the use of the immunogen of Claim 1, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

10. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 17 provides for the use of an immunogen, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

11. Claim 17 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-4, 7, 33 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Frangione-Beebe, *et al.* The claims are drawn to an immunogenic construct comprising a peptide derived from retroviral transmembrane protein (variously referred to as gp41, gp46, *etc.*). Further limitations are: The locations from which the sequences are derived (locations described as between transmembrane (TM) regions and first two helical regions), the nature of the construct (peptidyl or polynucleotides), the virus from which the construct were derived including the lentivirus family and gamma retroviruses, and that the linker is derived from another viral transmembrane protein. Frangione-Beebe, *et al.* teaches a HTLV-1 derived immunogenic construct (ACH-REF) comprising a peptide sequence including sequences between a TM region and the first helical region, the first and second helical regions, and a linker region between the two having sequence identity with a STLV-1 transmembrane protein. Thus, Frangione-Beebe, *et al.* teaches each and every limitation of the claims which are properly rejected under 35 U.S.C. 102(b).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 5, 6, 17, and 34 rejected under 35 U.S.C. 103(a) as being unpatentable over Frangione-Beebe, *et al.* in view of Salminen, *et al.* The claims are drawn to an immunogenic construct derived from viral transmembrane proteins as described above for claim 1; claims 5 and 34 limit the protein specie whereas claims 6 and 17 limit the amino acid sequence identity of a portion of the construct--each limitation includes sequences derived from HIV-1 gp41. Frangione-Beebe, *et al.* teaches the use of a recombinant protein, ACH-RE3, as an immunogen; ACH-RE3 was derived from amino acid residues of a mouse retrovirus and share regions of homology and identity with other retroviral transmembrane proteins. The sequence taught in Frangione-Beebe, *et al.* (and deposited in Gene Bank) includes portion upstream of the first ά-helix as well as downstream from the fusion region of the transmembrane protein. Frangione-Beebe, *et al.* does not teach sequences derived from HIV-1 gp41. Salminen, *et al.* teaches the sequences of several full-length HIV-1 clones including the sequence of gp41. SEQ ID No. 1 matches amino acid sequence 538-550 of one of the isolates and was submitted to Gene Bank under accession number AAB60578.1:

SEQ ID NO. 1	1	QARQLLSDIVQQQ	13
		QARQLLSDIVQQQ	
AAB60578.1	538	QARQLLSDIVQQQ	550

Thus, the combination of Frangione-Beebe, *et al.* and Salminen, *et al.* teaches each and every limitation of the claims.

A skilled artisan would have been motivated to combine the teachings of Frangione-Beebe, *et al.* and Salminen, *et al.* to produce immunogenic constructs directed against HIV-1 for research purposes. The skilled artisan would have had an expectation of success because the proteins are functionally equivalent, are derived from related retroviruses, and possess similar structural features. Thus, the claims are *prima facie* obvious over Frangione-Beebe, *et al.* in view of Salminen, *et al.* and properly rejected under 35 U.S.C. 103(a).

14. Claims 8 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frangione-Beebe, *et al.* in view of Laukkanen, *et al.* The claims are drawn to an immunogenic construct derived from viral transmembrane proteins as described above for claim 1; claims 8 and 37 further require an association, anchoring or trapping of the peptidyl immunogen in a liposomal membrane.

The teachings of Frangione-Beebe, *et al.* are summarized above; Laukkanen, *et al.* teaches a method for preparing peptidyl entities for inclusion in liposomal preparations by attaching a lipid to a portion of a synthetic antibody. The resultant antibody bearing liposomal preparation possessed multiple copies of the antibody on its surface that were functionally intact.

It would have been obvious for a skilled artisan to derivatize the immunogens of Frangione-Beebe, *et al.* with lipids for inclusion in liposomes. The skilled artisan would have a high expectation of success because of the success of Laukkanen,

et al. in inserting a complex protein in liposomes whilst retaining functional activity of the protein. The skilled artisan would have been motivated because of the well-known superiority of multimeric immunogens compared to their monomeric versions. Thus, the claims are *prima facie* obvious over Frangione-Beebe, *et al.* in view of Laukkanen, *et al.* and properly rejected under 35 U.S.C. 103(a).

15. Claims 13, 14, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frangione-Beebe, *et al.* in view of Andersson, *et al.* The claims are drawn to an immunogenic construct derived from viral transmembrane proteins as described above for claim 1; claims 13, 14 and 40 further require covalent linkage of the peptidyl immunogen with a carrier or adjuvant.
The teachings of Frangione-Beebe, *et al.* are summarized above; Andersson, *et al.* teaches a method for preparing peptidyl entities for inclusion into ISCOM preparations. The resultant immunogen-bearing ISCOM preparation possessed multiple copies of the antibody on its surface that were functionally intact.
It would have been obvious for a skilled artisan to derivatize the immunogens of Frangione-Beebe, *et al.* for inclusion into ISCOMS, as taught by Andersson, *et al.* The skilled artisan would have a high expectation of success because of the success of Andersson, *et al.* in inserting a complex protein immunogens into ISCOMS whilst retaining functional activity of the protein. The skilled artisan would have been motivated because of the well-known superiority of multimeric immunogens compared to their monomeric versions. Thus, the claims are *prima*

facie obvious over Frangione-Beebe, *et al.* in view of Laukkanen, *et al.* and properly rejected under 35 U.S.C. 103(a).

16. Claims 15 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Frangione-Beebe, *et al.* in view of Tian, *et al.* The claims are drawn to an immunogenic construct derived from viral transmembrane proteins as described above for claim 1; claims 15 and 41 further require covalent linkage of the peptidyl immunogen with a larger peptidyl entity including KLH.

The teachings of Frangione-Beebe, *et al.* are summarized above; Tian, *et al.* teaches a method for preparing peptidyl entities fused to KLH.

It would have been obvious for a skilled artisan to derivatize the immunogens of Frangione-Beebe, *et al.* with KLH, as taught by Tian, *et al.* The skilled artisan would have a high expectation of success because of the success of Andersson, *et al.* in fusing complex protein immunogens with KLH whilst retaining functional activity of the protein. The skilled artisan would have been motivated because of the well-known immunogenic superiority of immunogens attached to KLH compared to small immunogens not attached to KLH. Thus, the claims are *prima facie* obvious over Frangione-Beebe, *et al.* in view of Tian, *et al.* and properly rejected under 35 U.S.C. 103(a).

Conclusion

17. No claims are allowed.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to STUART W. SNYDER whose telephone number is (571)272-9945. The examiner can normally be reached on 9:00 AM-5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce R. Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mary E Mosher/
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Stuart W Snyder
Examiner
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